Solving a weighty problem: A systematic review and meta-analysis of nutrition interventions in severe mental illness

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Abstract

Background. Nutritional interventions would appear fundamental for weight management and cardiometabolic risk reduction in people experiencing severe mental illness (SMI). Comprehensive evaluation of nutritional interventions is lacking.

Purpose. Subject randomised-controlled trials of nutritional interventions in people experiencing SMI to systematic review and meta-analysis. Anthropometric and biochemical measures, and nutritional intake were measured.

Procedure. Electronic database search identified trials with nutritional intervention components. Trials were pooled for meta-analysis. Meta-regression analyses were performed on anthropometric moderators.

Main Findings. Interventions led to significant weight loss (19 studies, g=-0.39, p<0.001, I^2=55%), reduced BMI (17 studies, g=-0.40, p<0.001, I^2=51%), decreased waist circumference (10 studies, g=-0.27, p<0.001, I^2=17%) and lower blood glucose levels (5 studies, g=-0.37, p=0.02, I^2=68%). Dietitian-led interventions (six studies, g=-0.90, I^2=48%) and studies delivered at antipsychotic initiation (four studies, g=-0.61, I^2=34%) had larger effect sizes.

Conclusion. Evidence supports nutritional interventions as standard care in preventing and treating weight gain among people experiencing SMI.

Trial registration. PROSPERO Registration #CRD42014014017

Keywords: nutrition, diet, weight, intervention, psychosis, severe mental illness.

Introduction

People with severe mental illness (SMI) consume diets that are more energy dense, highly processed, higher in salt and contain less fruit and vegetables, compared to the general population [1]. People with SMI also engage in lower levels of physical activity [2] and have higher rates of smoking and substance use [3, 4]. Antipsychotic medications induce greatly increased hunger, decreased satiety, and increased cravings for sweet foods and drinks [5, 6]. Additionally, a number of adverse eating styles have been observed, including fast-eating syndrome, disordered eating habits (e.g. only eating one main meal daily), increased consumption of junk food, and low food literacy [5-7].

While the poor physical health of people with SMI is well established, consensus on the appropriate prevention and/or treatment interventions is in evolution, with calls for increased emphasis on lifestyle interventions aimed at reducing overweight/obesity and consequent metabolic abnormalities in established SMI [8], and preventing these adverse health trajectories in the early stages of psychosis [9, 10]. The mandate for improved physical health care and physical health protection in severe mental illness has led to an international working group and declaration, Healthy Active Lives (HeAL) that has established goals for the prevention of cardiometabolic decline in first episode psychosis (www.iphys.com.au) [11]. Strong evidence now exists for holistic lifestyle interventions [8], and as part of this the inclusion of physical activity interventions for people living with severe mental illness [12].

Poor physical health in people experiencing severe mental illness stems from both modifiable and non-modifiable risk factors linked to the illness itself, compounded by significant medication effects. Antipsychotic medications induce rapid weight gain with

associated metabolic abnormalities [13, 14]. This weight gain contributes to the high rates of overweight and obesity and metabolic complications in people with established SMI, with diabetes and hypercholesterolemia rates two and five-fold higher than that observed in the general population, respectively [15-18].

To date the efficacy of specific components, including modes of delivery, of nutrition interventions have not yet been systematically evaluated. With irrefutable evidence demonstrating the crucial role of nutrition in weight management [19] and the prevention and treatment of metabolic disease in the general population [20, 21], a comprehensive assessment of various nutritional intervention strategies employed to assist a highly vulnerable and challenging populations is a priority.

The specific questions to be answered by this review and meta-analysis of randomised-controlled trials (RCTs) include:

1. Do nutrition interventions improve anthropometric measures (weight, BMI and waist circumference) and biochemical profiles (lipids, glucose and insulin) of people living with a severe mental illness?
2. Do nutrition interventions improve the nutritional intake of people living with severe mental illness?

Methods

Design

The aims and methods of this systematic review and meta-analysis were registered with the PROSPERO database prior to conducting the review (CRD42014014017). Reporting has been conducted in accordance with the PRISMA statement [22].

Search Strategy

An electronic database search was completed from earliest record to February 2015 using MEDLINE, Embase, Cochrane Central Register of Clinical Trials, PsychINFO and CINAHL, using key nutritional, anthropometric and psychiatric terminology (see appendix 1 for search strategy). Google Scholar and relevant published systematic reviews were manually searched for additional titles. Study eligibility was assessed according to inclusion criteria by two investigators. If agreement was not established, a third investigator acted as arbitrator. Data were extracted by the two investigators and pooled for meta-analysis.

Assessment of Trial Characteristics and Risk of Bias

Quality. Trial quality was assessed using a modified version of the CASP (Critical Appraisal Skills Programme) Randomised Controlled Trial Checklist [23]. Trial characteristics were assessed across four criteria: (i) concealed allocation, (ii) assessor blinding, (iii) treatment equality between groups (excluding intervention), and (iv) accounting for all participants randomised and allocated one point for each (maximum score of four).

Participants. RCTs recruiting participants ≥ 18 years meeting Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Disease

(ICD) criteria for SMI (schizophrenia spectrum disorder, bipolar affective disorder, depression with psychotic features) were eligible for inclusion. There were no restrictions on medication use.

Interventions. Studies of stand-alone nutritional interventions or nutritional interventions delivered as part of a multidisciplinary intervention were included. Interventions comprising individualized nutritional counselling, group nutritional education, shopping or cooking classes were eligible. No restriction was placed on intervention setting: interventions in inpatient services, outpatient programs, and community volunteer services or otherwise were included. The process of referral to the study, location where the intervention was delivered, and the professional background of those who delivered the intervention were recorded. No restriction was placed on intervention intensity or duration.

Outcome Measures. All trials that met inclusion criteria were included in a qualitative analysis. Trials were included in the meta-analysis if they provided adequate data on anthropometric (primary outcome: weight, body mass index (BMI) and waist circumference (WC)), biochemical and/or nutritional parameters (secondary outcomes: total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, blood glucose, insulin and dietary intake). Data collection time points included pre- and post-intervention and follow-up. Where necessary, corresponding authors of included RCT's were contacted to provide additional data for inclusion in the meta-analysis. A follow-up and final email was sent three weeks later if corresponding authors did not reply to the initial request.

Data-analysis

Due to the anticipated heterogeneity, we utilised a random effects meta-analysis and calculated hedges *g* and 95% confidence intervals (CIs) as the effect size measure (ES). The meta-analysis was conducted in the following stages. First, we calculated hedges *g* and the 95% CI for the primary outcome measures (weight, BMI and waist circumference). Second, we conducted subgroup analyses to investigate differences in the primary outcomes for the main analysis according to a) if they were delivered by a dietitian or not and b) if they were delivered at antipsychotic initiation (≤3 months exposure to second-generation antipsychotic medication) or subsequent to antipsychotic use. For each subgroup analysis, we investigated the between subgroup difference in effect size and report the corresponding p value. Third, we conducted meta-regression analyses investigating potential moderators of the primary outcome results including; percentage of males and mean age in both control and intervention groups, percent receiving antipsychotics, duration of intervention, profession who delivered the intervention and exercise intensity. In order to test if the profession who delivered the intervention (dietitians versus other healthcare professionals) was an independent predictor of our primary outcomes from other variables (in particular exercise participation in multimodal programs) we conducted multivariate meta-regressions. In order to correct for multiple testing of covariates in our meta-regression, a Bonferroni correction was made and a new p value to indicate significance was set at 0.006 (0.05 divided by 8). In the next stage, we calculated the hedges *g* and 95% CI for the secondary outcomes including systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, blood glucose and insulin. We investigated heterogeneity with the I^2 statistic. Publication bias was assessed with a visual inspection of funnel plots and with the Begg-Mazumdar Kendall's tau [24] and Egger bias test [25]. If we encountered publication bias, we adjusted for this by conducting a trim and fill adjusted analysis [26]

to remove the most extreme small studies from the positive side of the funnel plot, and recalculated the effect size at each iteration, until the funnel plot was symmetric about the (new) effect size. All analyses were conducted with Comprehensive Meta-Analysis software (CMA; Version 3, Biostat, Englewood, New Jersey).

Results

Identification and Selection of Studies.

After accounting for duplicates 7,045 unique records were screened from the database searches. Full text articles were accessed for 176 records, 150 did not meet the inclusion criteria and were subsequently excluded with reasons (see figure 1 for details). Twenty-six studies met the inclusion criteria [27-52], however six studies reported incomplete data and could not be pooled for meta-analysis [31, 32, 36, 41, 46, 48]. For the primary outcomes measures, 19 studies were pooled for weight [27-30, 33-35, 37, 38, 40, 42-45, 47, 49-52], 17 studies for BMI [27-29, 33-35, 37, 39, 40, 42-45, 47, 50-52], and 11 studies for WC [28, 33-35, 37, 39, 40, 44, 47, 50, 52]. For secondary outcomes, eight studies were pooled reporting the impact of nutritional interventions on biochemical outcomes (blood pressure, lipids, glucose, insulin) [28, 29, 34, 37, 39, 42, 45, 47]. Measures of nutritional intake were reported in six studies [28, 31, 32, 38, 44, 46]. These measures could not be pooled for quantitative analysis, but were included in qualitative analysis. Longer term follow-up of two included studies were reported in separate publications [53, 54]. Comprehensive data sets were obtained directly from corresponding authors for two studies [37, 42]. Supplementary Figure 1 illustrates the PRISMA flow diagram.

Characteristics of Included Trials.

Participants. The sample size within studies ranged from n=15 to n=291. Mean participant age (SD) ranged from 26 ± 15.5 to 54.8 ± 8.2 years. Diagnoses within included studies were; schizophrenia (18 studies), schizoaffective disorder (12 studies), schizophreniform disorder (3 studies), bipolar affective disorder (7 studies), delusional disorder (2 studies), brief reactive psychosis (2 studies), psychosis not otherwise specified (2 studies), personality disorder (2 studies), anxiety (2 studies), and

depression (2 studies). First-episode psychosis, major affective illness, major depression disorder, psychotic depression and post-traumatic stress disorder were identified in one study each. More general diagnostic descriptors were also employed in a minority of studies; SMI (4 studies), psychosis (2 studies), schizophrenia spectrum (1 study) and autism spectrum (1 study). Participants were recruited from outpatient settings (21 studies), inpatient settings (3 studies), or included a mix of outpatients and inpatients (2 studies). Characteristics of included trials are summarized in Table 1.

Intervention. Nutritional intervention delivery method included individualised counselling (12 studies), group education (12 studies) and a mixture of group and individual components (2 studies). Seven studies primarily used dietitians to deliver interventions [33, 35, 42, 45, 48, 49, 52], with an additional five studies including a nutrition professional as a smaller part of the intervention primarily delivered by other clinicians [28, 30, 37, 41, 47]. Fourteen studies did not report input from a nutrition professional [27, 29, 31, 32, 34, 36, 38-40, 43, 44, 46, 50, 51]. Seven studies adopted a manual-based lifestyle intervention [27-29, 31, 32, 43, 50], predominantly delivered by mental health clinicians. Studies delivered predominantly by dietitians involved individualised assessment and intervention approaches. Other interventions included general nutrition education aimed at improving food literacy (not individualised counselling), weight management guidance and healthy-eating education. Cooking classes were reported in four studies [33, 36, 37, 41]. One study incorporated two meal replacements per day [30], and another solely assessed the impact of providing free fruit and vegetables to participant households [46].

All studies described strategies employed to alter participant behaviour, such as cue elimination, food diary/record keeping and food sampling, although the specific

behaviour change models utilised were more difficult to identify and interpret. Psychoeducation was described in seven studies [27, 28, 33, 43-45, 49]. Cognitive behaviour therapy and social cognitive therapy were identified in three studies [29, 42, 51] and one study respectively [34]. Within the cognitive framework, motivational interviewing and more generally motivational counselling/support were commonly utilised, [27, 28, 31, 32, 36, 37, 39, 44, 50]. In addition, the 'stages of change' model was described in two studies where motivational interviewing was used [39, 50]. Finally, one study described the use of behaviour self-management therapy [34]. Psychoeducation was combined with motivational counselling/support in three studies [27, 28, 44]. Control groups received treatment as usual with or without written physical health information.

Outcome Measures. Twenty-five studies assessed anthropometric measures, predominantly weight and BMI [27-45, 47-52]. Additional measures included WC, waist-to-hip ratio and body fat percentage. Eleven studies (42%) included biochemical outcome measures, predominantly lipids (cholesterol studies and triglycerides), glucose and insulin [28, 33, 34, 37, 39, 41, 42, 45, 47, 51, 52]. Studies including measures of nutritional intake were limited to six studies (25%) [28, 31, 32, 38, 44, 46], included energy (kilojoules/calories), serves of food groups (such as fruit and vegetables), macronutrients (including fat and subgroups unsaturated and saturated fat), fibre and portion size. In addition one study used a 'ten good food score' [44].

Trial Quality. Seven studies (27%) scored the maximum four points [27, 28, 31, 32, 34, 40, 44], four studies (15%) scored three [33, 36, 50, 51], thirteen studies (50%) scored two [29, 30, 37-39, 41-43, 45-48, 52], and two studies (8%) scored one [35, 49]. 'Group treatment equality' and 'all participants being accounted for' were reported in 25

studies (96%) and 22 studies (85%) respectively. Methodological uncertainties included 'concealed group allocation' and 'assessor blinding', described in 12 studies (46%) and nine studies (35%) respectively, (full details in supplementary table 1).

Meta-analysis results

Nutritional interventions impact on anthropometrics measures (Primary Outcomes).

Pooled analysis showed that nutritional interventions were significantly more effective in reducing weight versus control (19 studies) (g = -0.39, 95% CI -0.56 to -0.21, p<0.001, I^2 = 55%), (figure 2). There was evidence of publication bias (Begg = -0.41, p=0.01; Egger = -1.7, p=0.08) whilst the Duval and Tweedie trim and fill effect size adjusting for publication bias remained similar and statistically significant (g = -0.33, 95% CI -0.44 to -0.22).

Insert Figure 1 about here.

Nutritional interventions also reduced BMI compared to control groups (17 studies) (g = -0.39, 95% CI -0.56 to -0.22, p<0.001, I^2 = 51%), (see supplementary figure 2a). The results remained statistically significant when adjusted for publication bias in the trim and fill analysis (g = -0.34 (95% CI -0.45 to -0.23).

Nutritional interventions were also effective in reducing waist circumference versus control (11 studies) (g = -0.27, 95% CI -0.42 to – 0.12, p<0.001, I^2 = 17%), (see supplementary table 3). The results remained statistically significant in the trim and fill analysis (g = -0.25 (95% CI -0.38 to -0.12).

Subgroup analysis: At initiation of antipsychotic medication versus subsequent to antipsychotic use

A larger effect size was found for studies delivered at antipsychotic initiation (4 studies, *g* = -0.61, 95% CI -1.02 to = -0.18, p = 0.006, I^2 = 34%) compared to studies delivered subsequent to antipsychotic use (15 studies, *g* = -0.35, 95% CI -0.54 to -0.16, p<0.001, I^2 = 57%), (see supplementary figure 1). Similar results were seen for BMI (*g* = -0.56 versus g=-0.36) and waist circumference (g=-0.53 versus g=-0.23) (see supplementary figures 2a, 3b and 4b). Between group differences did not reach statistical significance after applying a Bonferroni correction. Full details of subgroup analyses are presented in table 2.

Subgroup analyses: Profession delivering intervention

Subgroup analysis investigating the effect of who delivered the nutritional intervention revealed that dietitians delivering specialized dietary interventions (6 studies), (hedges *g* = -0.90, 95% CI -1.22 to -0.58, p<0.001, I^2 = 48%) had a significantly larger (p=0.0005) effect compared to interventions predominantly delivered by other health professionals/ mental health clinicians (13 studies) (hedges *g* = -0.23, 95% CI -0.38 to -0.09, p=0.002, I^2 = 8%), (see supplementary figures 2b, 3c and 4c).

All of the meta-analyses results including subgroup analyses are presented in table 2.

Meta-regression analyses of primary outcomes

Weight

Single meta-regression analyses found that the profession delivering the intervention (dietitian versus other healthcare professionals (HCPs)), (β = -0.69, 95% CI -1.05 to -0.32, p<0.001) was a significant predictor of weight change. Multivariate regression

analysis found that the professional delivering the intervention (dietitians versus other HCPs) remained a significant predictor of weight change independent of exercise (β = -0.72, 95% CI -1.06 to -0.37, p<0.001). The percentage of males in the control group (β = 0.01, 95% CI 0.0 to 0.02, p=0.05), and percentage of males in the nutrition group (β = 0.02, 95% CI -0.0 to 0.03, p=0.01) were positive predictors of weight, (i.e. more difficult to lose weight).

Body Mass Index

A dietitian-delivered intervention was a significant moderator of BMI results (β = -0.53, 95% CI -0.9 to -0.16, p=0.005). This finding was confirmed through multivariate regression analysis and the results remained significant independent of exercise participation, (β = -0.52, 95% CI -0.85 to -0.20, p=0.001), with exercise not found to be a significant moderator (β = -0.21, 95% CI -0.44 to 0.02, p=0.07).

Waist circumference

There was a non-significant trend for dietitian-delivered interventions to moderate waist circumference results (β = -0.37, 95% CI -0.76 to -0.02, p=0.06). Multivariate regression analysis confirmed the trend for the profession delivering the intervention as a moderator independent of exercise intensity (β = -0.36, 95% CI -0.76 to -0.03, p=0.072).

All meta regression analyses are presented in table 3.

Meta-analyses of Nutritional interventions on Secondary Outcomes

The meta-analyses for the secondary outcomes are presented in table 2. The analyses demonstrated that nutritional interventions reduced glucose (*g* = -0.37, 95% CI -0.69 to

-0.05, p=0.02, I^2 = 68%, see supplementary figure 4), however this was not statistically significant after applying the Bonferroni correction. Triglycerides (*g* = -0.15, 95% CI -0.30 to 0.01, p=0.07, I^2 = 0%) were not significantly impacted by nutritional interventions, although trends were evident. Other secondary outcome measures were not significant (table 2).

Insert table 2 and table 3 about here

Impact on Nutritional Intake

Results for all six studies [28, 31, 32, 38, 44, 46], which assessed changes in nutritional intake, favoured the intervention group, however could not be pooled for meta-analysis due to the varying outcomes measured. Three studies utilised the Dietary Instrument for Nutrition Education (DINE) to assess fat (unsaturated and saturated) and fibre intake [28, 31, 32]. One study providing one hour, weekly discussion groups, which did not find significant changes in anthropometric measures, also did not find significant changes in fat or fibre [28]. Two studies delivered by key workers utilising a lifestyle manual, individually, which found small but significant improvements in anthropometric measures, found improvements in saturated fat and fibre intake [31], and improvements in saturated fat, fruit and vegetable intake [32]. One study utilised the Block Fruit, Vegetable, and Dietary Fat Screeners, to assess dietary change in an intervention providing healthy eating and weight-loss advice, delivered by research staff [38]. This study did not find significant differences in dietary behaviours. A fifth study utilised a food frequency questionnaire, which appears validated in women in the general population [44]. This food frequency questionnaire assessed the frequency of 10 foods associated with better diet and 10 foods associated with poorer diet, which through individual psycho-education and goal setting, significantly improved the score

of foods associated with good diet compared to control, but not the score of foods associated with poorer diet [44]. Finally, one trial involved using the Scottish Health Survey to assess whether providing free fruit and vegetables to families improved nutritional intake [46]. Although improvements in fruit and vegetable intake were found, these were not sustained after once the trial, and subsequently, access to free fruit and vegetables had ceased.

Discussion

To our knowledge, this is the first systematic review to assess the impact of key components that comprise, and modes of delivery of, nutrition interventions on physical health measures of people with severe mental illness. We found that nutrition interventions improved anthropometric measures by reducing weight, BMI and waist circumference. Importantly, it provided evidence about the most effective goals and delivery methods, including preventing weight gain from the initiation of antipsychotics, and qualified health professionals, such as dietitians, delivering individualised interventions. Our results indicated that nutritional interventions are most effective when delivered by a dietitian, with meta-regression analyses confirming this in multivariate models. These findings show a clear and important role for dietitians as part of the multidisciplinary mental health team.

Although the overall effect size for anthropometric measures was within the small to moderate range, it provided further evidence to support implementation of lifestyle interventions. While between group differences did not reach statistical significance, the larger effect size *(g* = -0.61) seen in a pooled analysis of studies providing intervention in the early stages of antipsychotic therapy, where weight gain is most rapid [13], provides evidence for the achievability of Goal 5 of the Healthy Active Lives Declaration (www.iphys.org.au) (that is, to restrict weight gain to no more than 7% of pre-illness weight in 75% of people experiencing first-episode psychosis, two-years after commencing antipsychotic treatment) [11]. Targeting interventions to coincide with antipsychotic initiation is also warranted given clinical benefits of preventing significant weight-gain and metabolic deterioration. Given the large effect size *(g* = -0.90) found for key anthropometric outcomes, nutritional interventions delivered by dietitians, in particular individualised counselling sessions, should play a central role in addressing

cardiometabolic abnormalities [18] and premature mortality in people with SMI [55].

It was not possible to conduct a meta-analysis on nutritional intake due to a lack of consensus on data collection methods together with the use of highly variable outcome measures. Nutritional intake can be notoriously difficult to assess accurately due to intake variability and wide ranging nutrients to consider, particularly if the assessment method is not targeted to the specific population. To date there is no validated nutrition assessment tool developed for use in people living with severe mental illness, a significant gap in the literature requiring urgent attention. In addition, improvements in cardiometabolic health as a result of changes in nutritional intake, independent of weight change, have not been assessed in this population. This is a significant area missing from the literature given the enduring weight challenges in this population.

Our results are broadly similar to previous non-pharmacological and physical activity intervention analyses completed by Alvarez-Jimenez et al. [56], Bruins et al. [57], and Rosenbaum et al. [12]. Effect sizes (ES) from these analyses on anthropometric measures were; *Z*=7.85 [56], ES=0.63 [57] and SMD=0.24 [12]. This is however the first review to consider the impact of nutritional interventions and provides further recommendations for dietitian-led interventions incorporated from the early stages in SMI. As with the general population, nutritional interventions are most likely to be effective when combined with physical activity.

Limitations and future research

Several factors may have influenced the results obtained by this review, largely reflecting limitations in the primary studies. First, nutrition interventions were often delivered as part of a comprehensive lifestyle programs, thus participants were

potentially receiving concomitant additional lifestyle interventions, such as physical activity, which may have had a synergistic effect on participant outcomes. Although it was not possible to separate the impact of the nutrition intervention from additional components, we attempted to investigate the impact of nutritional interventions through a series of adjustments for potential confounders. For instance, for the primary outcome, our multivariate meta-regression analyses consistently demonstrated that nutritional interventions were most effective when delivered by a dietitian, even when we adjusted for concomitant exercise elements. Whilst the results from our subgroup analyses consistently demonstrated higher effect sizes of dietitian-led nutritional interventions and interventions delivered at antipsychotic initiation, these findings did not reach statistical significance after applying the Bonferroni correction. Although, Bonferroni corrections are not routinely used in meta-analyses [58] we have opted for a conservative approach, and although our findings did not reach significance, they suggest more favourable outcomes and warrant further investigation. Second, the RCTs included a range of nutrition interventions including group education, individualised plans, practical shopping and cooking sessions, and meal replacements. Subgroup analysis were run where possible, however were limited by small numbers of studies and highly variable methods. Future research should seek to establish homogeneity in the use of appropriate outcome measures and nutritional interventions. Third, the potential for significant effects on relevant biochemical measures may have been impacted by the short duration of interventions in many studies and the target outcome measures being frequently limited to anthropometric measures. Future long term studies encompassing specific dietary strategies to target dyslipidaemia are required with adequate follow up to see the impact of nutritional interventions in this population [59]. Fourth, we did encounter some evidence of publication bias, but recalculated the effect sizes using Duval and Tweedies trim and fill method [26] and

our results were broadly similar. Fifth, we did encounter moderate heterogeneity in some of our analyses. Nonetheless, our multivariate meta-regression analyses explained all (R^2=1.0) of the observed heterogeneity for weight and BMI meta-analyses results. We were however, unable to explain the heterogeneity in waist circumference. High levels of variability and inaccuracies in waist circumference measuring may help explain the heterogeneity [60]. Finally, we were unable to access data from some of the identified studies, reducing the number of studies included and sample sizes included in some of the meta-analyses. In addition, some studies did not clearly identify the specific psychiatric diagnoses of participants, limiting the ability to draw further conclusions regarding the potential impact of diagnosis on the intervention outcomes obtained.

Nevertheless, allowing for these caveats, the results of this meta-analysis offer hope to clinical teams and patients alike that offering nutritional interventions as part of a wider multidisciplinary lifestyle intervention can be effective in preventing weight gain, particularly when delivered by a dietitian. University dietetic programs will also need to evolve to increase the knowledge and understanding of SMI.

Conclusion

Nutritional intake is fundamental to weight management and future physical health. This systematic review and meta-analysis found that nutritional interventions significantly improved weight, BMI, waist circumference and glucose levels in people with SMI. Further, nutritional interventions delivered by dietitians, and those aiming to prevent weight gain at antipsychotic initiation had the largest effect sizes. The evidence supports the early inclusion of nutritional intervention in mental health service delivery to people with SMI. Further RCTs are required to determine the most effective

nutritional intervention to optimise weight and cardiometabolic health in people with SMI.

Conflicts of Interest

None

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None

Contributions

Database searches were completed by ST with assistance from SR. Included trials were identified by ST and SR, with assistance from PBW. Data was extracted by ST and SR with assistance from BS, and confirmed by PBW. BS completed meta-analyses and meta regression analyses. Data was interpreted by ST and BS with assistance from all authors. ST led manuscript preparation. All authors added to the manuscript intellect and approved the final manuscript.

References

1. Dipasquale S, Pariante CM, Dazzan P, Aguglia E, McGuire P, Mondelli V. The dietary pattern of patients with schizophrenia: a systematic review. *J Psychiatr Res* 2013, **47**: 197-207.
2. Jerome GJ, Young DR, Dalcin A, Charleston J, Anthony C, Hayes J, et al. Physical activity levels of persons with mental illness attending psychiatric rehabilitation programs. *Schizophr Res* 2009, **108**: 252-7.
3. Cooper J, Mancuso SG, Borland R, Slade T, Galletly C, Castle D. Tobacco smoking among people living with a psychotic illness: The second Australian Survey of Psychosis. *Aust N Z J Psychiatry* 2012, **46**: 851-63.
4. Bahorik AL, Newhill CE, Queen CC, Eack SM. Under-reporting of drug use among individuals with schizophrenia: prevalence and predictors. *Psychol Med* 2014, **44**: 61-9.
5. Treuer T, Hoffmann VP, Chen AK, Irimia V, Ocampo M, Wang G, et al. Factors associated with weight gain during olanzapine treatment in patients with schizophrenia or bipolar disorder: results from a six-month prospective, multinational, observational study. *World J Biol Psychiatry* 2009, **10**: 729-40.
6. Blouin M, Tremblay A, Jalbert ME, Venables H, Bouchard RH, Roy MA, et al. Adiposity and eating behaviors in patients under second generation antipsychotics. *Obesity* 2008, **16**: 1780-7.
7. Yum SY, Caracci G, Hwang MY. Schizophrenia and eating disorders. *Psychiat Clin N Am* 2009, **32**: 809-19.
8. Bonfioli E, Berti L, Goss C, Muraro F, Burti L. Health promotion lifestyle interventions for weight management in psychosis: a systematic review and meta-analysis of randomised controlled trials. *BMC Psychiatry* 2012, **12**: 78.

9. Curtis J, Watkins A, Rosenbaum S, Teasdale S, Kalucy M, Samaras K, et al. Evaluating an individualized lifestyle and lifeskills intervention to prevent antipsychotic-induced weight gain in first-episode psychosis. *Early Interv Psychiatry* 2016; **10**: 267-76.

10. Teasdale S, Harris S, Rosenbaum S, Watkins A, Samaras K, Curtis J, et al. Individual Dietetic Consultations in First Episode Psychosis: A Novel Intervention to Reduce Cardiometabolic Risk. *Community Ment Health J* 2014; **11**: 211-4.

11. Shiers D, Curtis J. Cardiometabolic health in young people with psychosis. *Lancet Psychiatry* 2014; **1**: 492-4.

12. Rosenbaum S, Tiedemann A, Sherrington C, Curtis J, Ward PB. Physical activity interventions for people with mental illness: a systematic review and meta-analysis. *J Clin Psychiatry* 2014; **75**: 964-74.

13. Álvarez-Jiménez M, González-Blanch C, Crespo-Facorro B, Hetrick S, Rodríguez-Sánchez JM, Pérez-Iglesias R, et al. Antipsychotic-induced weight gain in chronic and first-episode psychotic disorders. *CNS Drugs* 2008; **22**: 547-62.

14. Correll CU, Manu P, Olshanskiy V, Napolitano B, Kane JM, Malhotra AK. Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents. *JAMA* 2009; **302**: 1765-73.

15. Miller BJ, Paschall CB, Svendsen DP. Mortality and medical comorbidity among patients with serious mental illness. *Psychiatr Serv* 2006; **57**: 1482-7.

16. Newcomer JW. Antipsychotic medications: metabolic and cardiovascular risk. *J Clin Psychiatry* 2006; **68**: 8-13.

17. Hennekens CH, Hennekens AR, Hollar D, Casey DE. Schizophrenia and increased risks of cardiovascular disease. *Am Heart J* 2005; **150**: 1115-21.

18. Vancampfort D, Stubbs B, Mitchell AJ, De Hert M, Wampers M, Ward PB, et al. Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis. *World Psychiatry* 2015; **14**: 339-47.

19. Franz MJ, VanWormer JJ, Crain LL, Boucher JL, Histon T, Caplan W, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J Am Diet Assoc* 2007; **107**: 1755-67.

20. Ajala O, English P, Pinkney J. Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes. *Am J Clin Nutr* 2013; **97**: 505-16.

21. Yamaoka K, Tango T. Effects of lifestyle modification on metabolic syndrome: a systematic review and meta-analysis. *BMC Med* 2012; **10**: 138.

22. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009. **151**: 264-9.

23. Critical Appraisal Skills Programme (CASP). *CASP Randomised Controlled Trial Checklist*. CASP, 2014. http://www.casp-uk.net/#!casp-tools-checklists/c18f8

24. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994; **50**: 1088-101.

25. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; **315**: 629-34.

26. Duval S, Tweedie R. Trim and fill: a simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000; **56**: 455-63.

55. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA Psychiatry* 2015; **72**: 334-41.

56. Alvarez-Jiménez M, Hetrick SE, González-Blanch C, Gleeson JF, McGorry PD. Non-pharmacological management of antipsychotic-induced weight gain: systematic review and meta-analysis of randomised controlled trials. *Br J Psychiatry* 2008; **193**: 101-7.

57. Bruins J, Jörg F, Bruggeman R, Slooff C, Corpeleijn E, Pijnenborg M. The Effects of Lifestyle Interventions on (Long-Term) Weight Management, Cardiometabolic Risk and Depressive Symptoms in People with Psychotic Disorders: A Meta-Analysis. *PloS One* 2014; **9**: e112276.

58. The Cochrane Collaboration. *Cochrane Handbook for Systematic Reviews of Interventions*. The Cochrane Collaboration, 2011. http://handbook.cochrane.org/chapter_16/16_7_2_multiplicity_in_systematic_reviews.htm

59. Huang J, Frohlich J, Ignaszewski AP. The impact of dietary changes and dietary supplements on lipid profile. *Can J Cardiol* 2011; **27**: 488-505.

60. Panoulas VF, Ahmad N, Fazal AA, Kassamall RH, Nightingale P, Gitas GD et al. The inter-operator variability in measuring waist circumference and its potential impact on the diagnosis of the metabolic syndrome. *Postgrad Med J* 2008; **84**: 344-7.

Table 1. Characteristics of included studies

Trial	Age (SD)		Diagnoses	Source from population	Delivered by	Delivery method	Nutrition intervention	Additional components	Control	Outcome(s)	Trial Quality^
	Active	Control									
Alvarez-Jimanez et al, 2006 [27] N = 61	26 (15.5)	27.5 (8.5)	SCZ, SAD, SCZF, DD, BRP, PNOS	Outpatient	Clinical psychologist, nurse	Individual	Conducted according to set lifestyle manual	Exercise program	Usual care	Wt, BMI	4
Attux et al, 2013 [28] N = 160	36.2 (9.9)	38.3 (10.7)	SCZ spectrum	Outpatient	Nurse, occupational therapist, clinical psychologist, dietitian	Group	Conducted according to set lifestyle manual	Education: physical activity, anxiety and self-esteem management	Usual care	Wt, BMI, WC, BP Lipids, glucose DINE	4
Brar et al, 2005 [29] N = 71	40 (10.1)	40.5 (10.6)	SCZ, SAD	Mixed	Group leader	Group	Conducted according to set lifestyle manual	Education: exercise to burn calories	Usual Care + encouraged to lose weight individually	Wt, BMI, WC, WHR	2
Brown et al, 2006 [31] N = 17	45.1	41.7	SMI	Outpatient	Key worker	Individual	Conducted according to set lifestyle manual	Education: exercise, daily activity and substance misuse	Usual care + health package post study	Wt, BMI, BP DINE	4
Brown et al, 2009 [32] N = 26	50.4	47	Psychosis, MAI, PD	Outpatient	Key worker	Individual	Conducted according to set lifestyle manual	Access to smoking cessation clinic and gym	Usual care + health package post study	Wt, BMI, BP DINE	4
Brown et al, 2011 [30] N = 89	44.6 (10.9)		SMI	Outpatient	Nurse, occupational therapist or dietitian	Individual	Twice daily meal replacements + education + goal setting	Exercise program	Usual care	Wt	2
Cordes at al, 2014 [33] N = 25	43.6 (6.9)	39.9 (12.7)	SCZ, SAD	Inpatient	Dietitian	Group	Healthy isocaloric diet education, practical shopping + cooking class	Exercise education module	Usual Care	Wt, BMI, WC BP Fasting lipids, glucose	3
Daumit et al, 2013 [34] N = 291	46.6 (11.5)	44.1 (11)	SMI	Outpatient	Community health educator	Individual + group	Weight management sessions	Group exercise sessions	Usual Care + standard nutrition and physical activity information	Wt, BMI, WC BP, lipids Glucose, insulin	4
Evans et al, 2005 [35] N = 34	34.6 (9.6)	33.6 (11.6)	SCZ, SAD, SCZF, BAD, DEP	Mixed	Dietitian	Individual	Best practice dietetic intervention	N/A	Usual Care + nutrition education booklet	Wt, BMI, WC	1
Forsberg et al, 2010 [36] N = 41	39.8	42.8	SCZ, BAD, PD, other psychotic disorders, autism spectrum	Outpatient	Not specified	Group	Theoretical diet training within practical shopping & cooking sessions	Physical activity sessions; substance use education	Usual care + art group sessions	Psychological outcome measures only	3
Gillhoff et al, 2010 [37] N = 50	48.1 (11.5)	48.9 (12)	BAD	Outpatient	Psychotherapist/ psychiatrist, nutrition counselor, fitness trainer	Group	Nutrition advice & cooking classes	Individual physical activity training; stress & symptom management	Usual care + intervention post study	Wt, BMI, WC, BP Blood lipids, HbA1c	2
Goldberg et al, 2013 [38] N = 109	50.5 (9.9)	53.5 (8.1)	SCZ, SAD, BAD, MDD,	Outpatient	Research staff	Individual + group	Healthy eating & weight loss education	Exercise education	Usual care + nutrition and	Wt, Diet	2

			PTSD, severe anxiety disorder						exercise information brochures		
Hjorth et al, 2014 [39] N = 97	M: 48.0 (13.6) F: 47.8 (11.1)	M: 41.5 (12.4) F: 45.0 (17.9)	SMI	Inpatient	Project leader + research nurse	Individual + group	Stage of Change + Motivational Interviewing, focus groups (patients + staff) & education sessions (staff)	Smoking cessation, physical activity encouragement	Usual care + individual sessions post study	Wt, BMI, WC, body fat %, BP Lipids, glucose	2
Iglesias-Garcia et al. 2010 [40] N = 15	Not specified		SCZ	Outpatient	Psychiatric nurse	Group	Structured information given to participants plus group discussion	Exercise/healthy habits and self-esteem	Usual care with weekly anthropometric measures	Wt, BMI, WC BP	4
Jean-Baptise et al, 2007 [41] N = 18	52.4	40.7	SCZ, SAD	Outpatient	Dietitian, psychiatrist	Group	Nutrition education sessions based on national standards, food provision, grocery store visit + cooking demonstration.	Physical activity encouraged, pedometers given	Usual care followed by intervention (cross-over design)	Wt, BP Fasting lipids, glucose	2
Kwon et al, 2006 [42] N = 39	32 (9.4)	29.8 (6.1)	SCZ, SAD	Outpatient	Dietitian + exercise coordinator.	Individual	Best practice dietetic intervention.	Exercise education + activity diary	Usual care + verbal recommendations for physical activity and eating behaviour	Wt, BMI Lipids, glucose	2
Littrell et al, 2003 [43] N = 70	33.7 (9.2)	34.5 (10)	SCZ, SAD	Outpatient	Master's-level clinician (nurse)	Group	Psychoeducation class using set lifestyle manual.	Fitness and exercise education module	Usual care	Wt, BMI	2
Lovell et al, 2014 [44] N = 105	25.6 (5.5)	25.9 (6)	SCZ, SAD, SCZF, DD, BRP, PNOS, FEP	Outpatient	Support, time and recovery workers	Individual	Psychoeducation plus patient-centered goals + action plan.	Optional sports groups	Usual care	Wt, BMI, WC FFQ	4
Mauri et al, 2008 [45] N = 33	38.9		SAD, BAD, Psychotic DEP	Outpatient	Dietitian	Individual	Psychoeducation with individualised diet and food diary.	Step counter with aim of reaching 10,000 steps	Usual care followed by intervention post study (cross-over design)	Wt, BMI Lipids, glucose, insulin	2
McCreadie et al, 2005 [46] N =	45 (13)		SCZ	Outpatient	Occupational therapist, case workers	Group (house)	Free fruit + vegetables +/- associated instructions	N/A	Usual care	Scottish Health Survey-fruit, vegetables, global assessment of diet + individual nutrients	2
McKibbin et al, 2006 [47] N = 57	53.1 (10.4)	54.8 (8.2)	SCZ	Outpatient	Not specified	Group	Psychoeducation on diabetes, nutrition and lifestyle education	Exercise education with pedometer	Usual care + diabetes education brochures	Wt, BMI, WC, BP Lipids, glucose	2
Milano et al, 2007 [48] N = 36	46	45	SCZ, BAD	Outpatient	Not specified	Individual	Nutrition counseling with specified diet including calorie reduction and nutritional balance	Physical activity program	Usual care with regular diet and no physical activity	Wt, BMI	2
Scocco et al, 2005 [49]	51.7	39.3 (9.9)	SCZ, SAD	Outpatient	Dietitian	Individual	Education, food diary,	Non-structured	Usual care +	Wt, BMI	1

N = 17	(12.4)						energy deficit	exercise with tailored advice	intervention post study		
Usher et al, 2012 [50] N = 101	Not specified		SCZ, BAD, DEP, Anxiety	Outpatient	Nurse	Group	Nutrition education in accordance with lifestyle booklet	Exercise education plus pedometer	Usual care + healthy lifestyle booklet	Wt, BMI, WC	3
Weber et al, 2006 N = 15	Not Specified		SCZ, SAD	Outpatient	Nurse	Group	Cognitive/behavioral lifestyle intervention	Exercise education plus activity diary	Usual care	Wt, BMI, WHR Glucose	3
Wu et al, 2007 N = 53	42.2 (7.5)	39 (6.7)	SCZ	Inpatient	Dietitian	Individual	Dietary plan with caloric restriction and nutritional balance	Exercise program	Usual care	Wt, BMI, WC, WHR, body fat % Lipids, glucose, insulin	2

* SCZ = Schizophrenia, SAD = Schizoaffective disorder, SCZF = Schizophreniform disorder, BAD = Bipolar affective disorder, DD = Delusional disorder, BRP = Brief reactive psychosis, PNOS = Psychosis not otherwise specified, MAI = Major affective illness, PD = Personality disorder, SMI = Severe mental illness, MDD = Major depression disorder, DEP = Depression, FEP = First-episode psychosis, PTSD = Post traumatic Syndrome Disorder, Wt = Weight, BMI = Body mass index, WC = Waist circumference, WHR = Waist-to-hip ratio, BP = Blood pressure, FFQ = Food Frequency Questionnaire, DINE = Dietary Instrument for Nutrition Education, HbA1c = Glycated haemoglobin. ^ Criteria used for trial quality scores included (i) concealed allocation, (ii) assessor blinding, (iii) group treatment equality, and (iv) all participants accounted for. Individual scoring for each trial is available in Supplementary Table 1.

Figure 1. Effect of nutritional interventions on weight (kg) versus control in RCTs

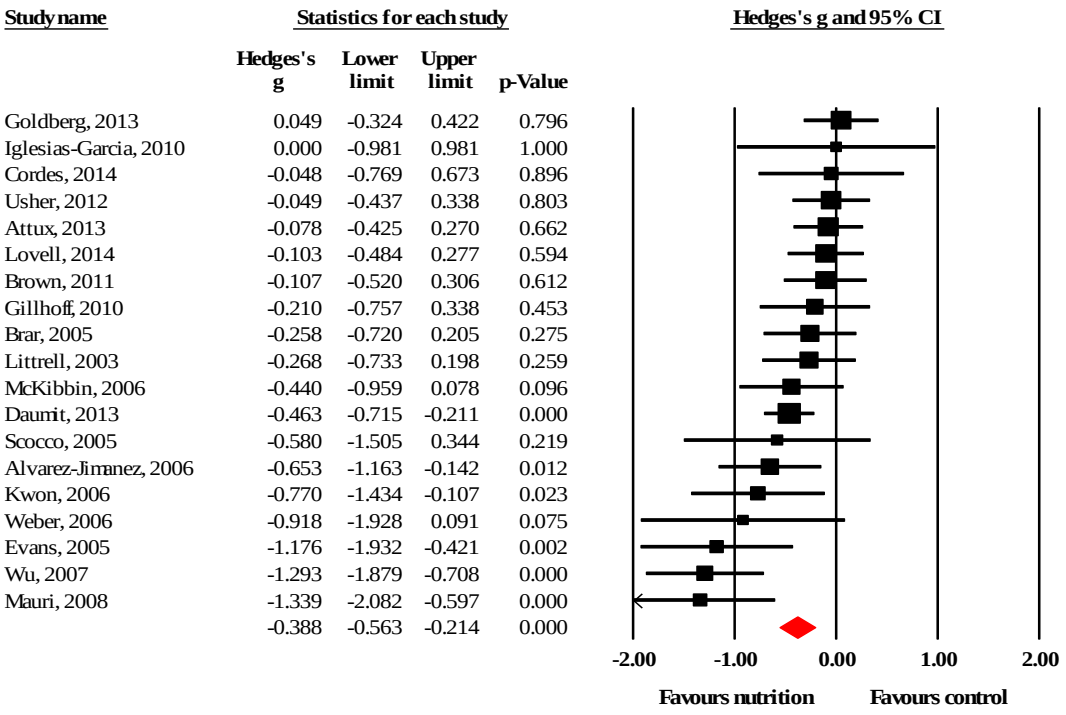

Table 2. Meta-analysis of primary, secondary and subgroup outcomes.

Analysis	**Number of RCTs**	**Meta-analysis of mean differences**					**Meta-analysis of Hedges' G**					**Heterogeneity**
		Mean difference	**95% CI**		**P value**	**Between group p value**	**Hedges g**	**95% CI**		**P value**	**Between group p value**	**I2**
Primary outcomes												
Weight (kg)	19	-2.706	-3.347	-2.064	**<0.001**		-0.388	-0.563	-0.214	**<0.001**		55%
Stage of antipsychotics						0.70					0.27	
At antipsychotic initiation	4	-2.948	-4.381	-1.515	**<0.001**		-0.613	-1.051	-0.175	**0.006**		34%
Subsequent to antipsychotic use	15	-2.639	-3.396	-1.883	**<0.001**		-0.345	-0.533	-0.158	**<0.001**		57%
Delivered by						0.02					**<0.001**	
Dietitian / nutrition professional	6	-3.577	-4.560	-2.594	**<0.001**		-0.904	-1.217	-0.577	**<0.001**		48%
Other healthcare profession	13	-2.060	-2.906	-1.214	**<0.001**		-0.233	-0.379	-0.088	**0.002**		8%
BMI (kg/m^2)	17	-0.870	-1.119	-0.621	**<0.001**		-0.390	-0.560	-0.221	**0.001**		51%
Stage of antipsychotics						0.73					0.40	
At antipsychotic initiation	3	-0.953	-1.506	-0.400	**<0.001**		-0.559	-0.986	-0.132	0.01		66%
Subsequent to antipsychotic use	14	-0.843	-1.136	-0.550	**<0.001**		-0.359	-0.547	-0.172	**<0.001**		50%
Delivered by						0.02					**<0.001**	
Dietitian / nutrition professional	5	-1.228	-1.589	-.0866	**<0.001**		-0.799	-1.106	-0.419	**<0.001**		69%
Other healthcare profession	12	-0.655	-0.943	-0.368	**<0.001**		-0.253	-0.410	-0.096	**0.002**		0%
Waist circumference (cm)	11	-2.281	-3.267	-1.296	**<0.001**		-0.267	-0.415	-0.118	**<0.001**		17%
Stage of antipsychotics						0.07					0.41	
At antipsychotic initiation	2	-4.189	-6.500	-1.878	**<0.001**		-0.532	-0.940	-0.124	0.011		82%
Subsequent to antipsychotic use	9	-1.857	-2.947	-0.768	**<0.001**		-0.225	-0.375	-0.074	**0.003**		0%
Delivered by						0.03					**0.006**	
Dietitian / nutrition professional	3	-4.223	-6.257	-2.189	**<0.001**		-0.575	-0.939	-0.211	**0.002**		68%
Other healthcare profession	8	-1.685	-2.182	-0.559	**0.003**		-0.206	-0.346	0.067	**0.004**		0%
Secondary outcome measures												
Systolic BP (mmHg)	7	0.632	-1.857	3.122	0.619		0.054	-0.179	0.286	0.651		54%
Diastolic BP (mmHg)	6	-1.686	-3.603	0.231	0.08		-0.232	-0.500	-0.037	0.091		61%
Glucose (mmol/L)	5	-0.473	-0.915	-0.030	0.04		-0.372	-0.692	-0.053	0.022		68%

Total Cholesterol (mmol/L)	7	-0.131	-0.288	0.027	0.103		-0.130	-0.286	0.029	0.101		0%
LDL Cholesterol (mmol/L)	7	-0.061	-0.168	0.045	0.259		-0.091	-0.248	0.067	0.258		0%
HDL Cholesterol (mmol/L)	7	-0.060	-0.158	0.042	0.239		-0.087	-0.243	0.069	0.272		0%
Triglycerides (mmol/L)	7	-0.116	-0.249	0.018	0.089		-0.146	-0.304	0.011	0.069		0%
Insulin (mU/ml)	3	-0.880	-2.652	0.892	0.330		-0.195	-0.426	0.035	0.097		18%

Key: BMI = Body Mass Index; BP = blood pressure. After applying the Bonferroni correction, the new p-value to signify significance was set at p=0.006.

Table 3. Meta-regression of moderators of primary outcomes (Weight, BMI, Waist circumference).

	Moderator	β	95% CI		P value	R^2
Weight						
	Mean age control group	0.0073	-0.0119	0.0265	0.456	0.06
	Mean age nutrition group	0.0016	-0.0179	0.021	0.874	0.00
	Percent males control group	0.0111	0.0003	0.022	**0.045**	0.41
	Percent males nutrition group	0.0145	-0.0033	0.0257	**0.012**	0.67
	Duration of intervention	0.0028	-0.0061	0.0118	0.536	0.00
	Profession delivering intervention	-0.6846	-1.0497	-0.3195	<**0.001**	0.82
	Multivariate: *Profession delivering intervention* *Exercise intensity*	-0.719 -0.18	-1.0642 -0.3994	-0.3738 0.0395	<**0.001** 0.108	1.00
BMI						
	Mean age control	0.0022	-0.017	0.0213	0.826	0.00
	Mean age nutrition group	-0.0015	-0.0196	0.0166	0.868	0.09
	Percent males control group	0.0097	-0.0033	0.0227	0.145	0.21
	Percent males nutrition group	0.0091	-0.0036	0.0218	0.161	0.20
	Duration of intervention	0.0033	-0.0045	0.0111	0.403	0.00
	Profession delivering intervention	-0.528	-0.8959	-0.1601	**0.005**	0.59
	Multivariate: *Profession delivering intervention* *Exercise intensity*	-0.5258 -0.208	-0.8478 -0.4347	-0.2038 0.0188	**0.001** 0.072	1.00
Waist circumference						
	Mean age control	-0.0089	-0.0271	0.0093	0.340	0.00
	Mean age nutrition group	-0.0096	-0.0272	0.008	-1.07	0.00
	Percent males control	0.0029	-0.0143	0.02	0.742	0.00
	Percent males nutrition group	0.0061	-0.0053	0.0176	0.291	0.00
	Duration of intervention	0.0005	-0.0046	0.0056	0.859	0.00
	Profession delivering intervention	-0.3692	-0.7592	0.0207	0.064	0.00
	Multivariate: *Profession delivering intervention* *Exercise intensity*	-0.3646 0.0164	-0.762 -0.2585	-0.0327 0.2913	0.072 0.907	0.00